

**REMARKS**

Reconsideration is requested.

Consideration of the attached art, which is listed on the attached PTO 1449 Form, and acknowledgement of the same by return of an initialed copy of the PTO 1449 Form, pursuant to MPEP § 609, are requested. The attached RCE is being filed to ensure entry and consideration of the attached art and the present Amendment.

Claims 1-16, 21-22, 27-30, 32, 36 and 37 have been canceled without prejudice. Claims 17-20, 23-26, 31 and 33-35 are pending. Claims 38-52 have been added.

Upon entry of the present Amendment, claims 17-20, 23-26, 31, 33-35 and 38-52 will be pending.

The Examiner interview of January 8, 2008, is acknowledged, with appreciation. The Examiner's Interview Summary is accurate in its brief description of the substance of the interview. The Examiner is understood to have indicated that the above amendments, which were discussed with the Examiner during the interview, may raise new issues requiring further search. The attached RCE is being filed, in part, to ensure entry of the present Amendment. The Examiner is again requested to contact the undersigned to arrange a personal interview at a time convenient for the Examiner and the Examiner's Supervisor which is prior to the Examiner mailing a further Action on the merits. See Amendment filed September 6, 2007.

As discussed with the Examiner during the interview, the claims have been revised, without prejudice, to define patentable aspects of the disclosure. Specifically, the claims involve the use of antibodies directed against an intermediate and a carboxy-terminal region of PTHrP, as described, for example, at page 1, lines 33-34,

page 27, lines 1-2, and the Examples related to Figures 6 and 8 of the specification. No new matter has been added.

To the extent not obviated by the above amendments, the Section 103 rejection of claims 17-20, 23-26, 31 and 33-35 over Ogata (EP 1 197 225), Iwamura (Cancer, 1999, Vol. 86, No. 6, pages 1028-1034), and Burton (BBRC, 1990, Vol. 167, No. 3), is traversed. Reconsideration and withdrawal of the rejection are requested in view of the following comments.

As discussed with the Examiner during the interview, the applicants believe that the cited art teaches away from the use of an antibody of the present claims to treat cancer. Specifically, the antibodies of the claims are directed against an intermediate region of PTHrP or a carboxy terminal region of PTHrP. The cited art however, such as Iwamura, teach that the intermediate and carboxy terminal regions of PTHrP have growth inhibitory activity against SKRC-1 cells. See page 1032, right column, lines 8-14 of Iwamura. It would have been contrary to Iwamura therefore to have treated a cancer with an antibody directed against these regions as to do so would have been expected to reduce the availability of the protein to act as a growth inhibitor.

There is nothing in Ogata or Burton to overcome the negative teaching of Iwamura.

The claims provide a method for treating a kidney cancer comprising the administration to a subject of an effective dose of a PTHrP antagonist for inhibiting or decreasing tumor growth or a pharmaceutical composition containing it, said PTHrP antagonist being an anti-PTHrP antibody directed against an intermediate region of PTHrP or a carboxy terminal region of PTHrP.

As recognized by the Examiner, Ogata et al fail to teach treating kidney cancer.

See page 4 of the Office Action dated June 8, 2007.

Ogata teaches treatment of diseases caused by PTH or PTHrP. Ogata describes diseases caused by PTH or PTHrP as including

"... a syndromes associated with malignancy caused by PTHrP (e.g. digestive system disorders such as diarrhea, vomituration and nausea), proteometabolism abnormality (e.g. hyperalbuminemia) saccharometabolism, abnormality (e.g. reduction of glucose tolerance and reduction of insulin secretion), lipid metabolism abnormality (e.g. hyperlipidemia and reduction of serum lipoprotein lipase activity), anorexia, hematological abnormality (e.g. anemia, thrombosis and DIC syndrome), electrolyte abnormality (e.g. hyponatremia, hypokalemia and hypercalcemia), immunodeficiency (e.g. infection disease), pain, secondary hyperparathyroidism and primary hyperthyroidism which are caused by PTH, etc.

Furthermore, the present invention provides an improving agent for the central nervous system disease caused by PTH or PTHrP, which comprises, as an active ingredient, an agonist or antagonist being to a PTH receptor or PTHrP receptor, or a substance binding to a ligand of the receptor to promote or inhibit binding between the ligand and the receptor. Examples of central nervous system diseases may include dyssomnia, neuropathy (e.g. schizophrenia, manic-depressive psychosis, neurosis and psychophysiologic disorder), nervous system (e.g. vomituration, nausea, mouth dryness, anorexia and vertigo), brain metabolism abnormality, cerebral circulation abnormality, autonomic imbalance, and endocrine system abnormality with which central nervous system is associated, etc." See page 3, ¶ [0016]-[0017] of Ogata.

Kidney cancer is not specifically recited or suggested in the detailed list of diseases described by Ogata.

The Examiner describes Example 4 of Ogata as relating to the administration of a humanized monoclonal anti-PTHrP antibody "to a rat cancer model". Id. Ogata is not believed to disclose any specific region against which the antibody is directed.

Moreover, the model of Example 4 of Ogata involved implantation of human large cell lung carcinoma LC-6, to nude rats. The implanted lung carcinoma is described in Ogata as producing PTHrP which manifested in irregular autonomic movement in the untreated rats. Ogata teaches that administration of an anti-PTHrP monoclonal antibody improved the effect of high PTHrP-related hypercalcemia on the central nervous system of the rats implanted with a human large cell lung carcinoma. Ogata therefore is not believed to describe or suggest any treatment of kidney cancer.

Burton et al. is understood to only concern studies carried out in vitro. At best, Burton is understood to involve the use of an uncharacterized polyclonal PTHrP antiserum, which is not believed to suggest the presently claimed invention. The applicants believe that a person of ordinary skill in the art would not have expected to have successfully made the presently claimed invention from the teachings of Burton, Ogata and Iwamura.

Withdrawal of the Section 103 rejection is requested.

The claims are submitted to be in condition for allowance and a Notice to that effect is requested.

The Examiner is again requested to contact the undersigned to arrange a personal interview at a time convenient for the Examiner and the Examiner's Supervisor which is prior to the Examiner mailing a further Action on the merits.

MASSFELDER et al.  
Appl. No. 10/520,085  
January 10, 2008  
AMENDMENT AFTER FINAL REJECTION

Respectfully submitted,

**NIXON & VANDERHYE P.C.**

By:                     /B. J. Sadoff/                      
B. J. Sadoff  
Reg. No. 36,663

BJS:  
901 North Glebe Road, 11th Floor  
Arlington, VA 22203-1808  
Telephone: (703) 816-4000  
Facsimile: (703) 816-4100